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Association of Serum 25- Hydroxyvitamin D with dyslipidaemia in Egyptian School Children

[1]Abu Shady M.M., [1]Mai M. Youssef, [1]Hala S. Megahed, [1]Samar M. Salem, [1]Ebtissam M. Salah, [2]Hanaa Wafay and [2]Hoda A. Megahed

[1]Child Health Department, [2]Medical Biochemistry Department, Medical Division, National Research Centre, Cairo (EGYPT).

Abstract: Background: Childhood dyslipidemia is associated with the risk of developing CVD in adulthood. Vitamin D deficiency has been reported as a risk factor for dyslipidaemia in adults.There are sparse epidemiologic data evaluating that association in children and adolescents. Objective: To evaluate the association between vitamin D deficiency and blood lipids among school children aged between 9 through 11 years. Subjects and methods: A cross-sectional study comprised 215 children; 80 boys and 135 girls. They were Pre- pubescent (tanner stage 1) aged from 9 to 11 years. The pupils were recruited from two primary public schools situated in Giza governorate in Egypt. Children were subjected to thorough clinical examination.The anthropometric data collected were weight and height, from which the body mass index (BMI) and BMI z-score were calculated. Serum samples were assayed for 25-hydroxy vitamin D (25(OH) vitamin D),total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides. Results:Our results showed statistically significant inverse association of serum OH vitamin D with BMI, serum cholesterol, triglyceride and LDL-cholesterol and direct association with HDL cholesterol. Also, results showed significant increased odds ratio for hypercholesterolemia, hypertriglyceridemia , and high low density lipoprotein, in subjects with serum OH vitamin D less than 30 ng/ml compared with those with normal serum OH vitamin D after adjustment for sex and BMI (2.912, 95% CI=1.561 – 5.435, OR=2.043, 95% CI=1.115 – 3.744, OR=4.292,95%CI=1.928 – 9.554 respectively).For low high density lipoprotein in the deficient group of vitamin D, the odd ratio was also significantly high (2.702, 95%CI=1.401 – 5.211) but after adjustment for sex and BMI no significant association was found (OR=1.784, 95%CI=0.927-3.433). Conclusion: We found that children and adolescents with varying levels of vitamin D deficiency had significantly increased risk of high total cholesterol, triglyceride and low density lipoprotein. Findings can inform more aggressive lifestyle and dietary interventions with vitamin D supplementation to reduce the risk of dyslipidemia in high risk children.

Key words: vitamin D deficiency, dyslipidemia, children, adolescents.

INTRODUCTION

Insufficient serum vitamin D level (< 30 ng/ml or < 75 nmol/L) is a common problem worldwide (Peterlik, *et al.,* 2009). Although sun exposure is the major source of vitamin D, several reports show that low vitamin D is common in sunny regions (Levis, *et al*., 2005). Despite the sunshine, Middle Eastern populations showed a high rate of low vitamin D due to limited sun exposure based on cultural practices(Baroncelli, *et al.,* 2008; El-Hajj Fuleihan, *et al*, 1999).

It has been estimated that 1 billion people worldwide have vitamin D deficiency or insufficiency (Holick, *et al*, 2006). Children and young adults are potentially at high risk for vitamin D deficiency. For example, 52% of Hispanic and black adolescents in a study in Boston (Gordon, *et al*., 2004) and 48% of white preadolescent girls in a study in Maine had 25-hydroxyvitamin D levels below 20 ng per millilitre (Sullivan, *et al*., 2005). In studies in Saudi Arabia, the United Arab Emirates, Australia, Turkey, India and Lebanon, 30 to 50% of children and adults had 25-hydroxyvitamin D levels under 20 ng per millilitre (Sedrani, *et al.,* 1984; Marwaha, *et al*., 2005; El-Hajj Fuleihan, *et al*., 2001; McGrath, *et al*., 2001).

Vitamin D has been reported to play a role in decreasing the risk of many chronic illnesses, including common cancers, autoimmune diseases, infectious diseases, and cardiovascular disease (Holick, *et al.,* 2007).

The issue on the association of serum 25-hydroxyvitamin D (OHVD) levels with insulin resistance and metabolic syndrome has become a subject supported and challenged by increasing reports of evidence as well as controversy. With increasing reports on the role of vitamin D on elements of diabetes and metabolic syndrome such as adiposity, glucose homeostasis, lipid profiles and blood pressure, further investigation for evidence is greatly encouraged (Alvarez, *et al*., 2010; Lee, *et al*., 2009 Ozfirat, 2010; Pittas, *et al*., 2010). There are several possible mechanisms contributing to the association between vitamin D and CVD, such as insulin sensitivity,

Corresponding Author: Abu shady MM, Child Health Department,National Research Centre, Cairo EGYPT.

parathyroid hormone elevation and inflammation (Zittermann, *et al*., 2005). The exact mechanisms by which vitamin D deficiency influences dyslipidemia have not been fully elucidated (Johnson, *et al*., 2009).

It is reasonable that dyslipidemia could also be considered as a potential link between vitamin D deficiency and CVD, because dyslipidemia is a well-described independent risk factor for CVD. Observational studies have indicated that high 25-hydroxyvitamin D [25(OH) D] levels were associated with a favorable serum lipid profile (Jorde, *et al*., 2011). Dyslipidemia is a metabolic disorder of lipoprotein metabolism which results in abnormal excesses of: total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), or triglycerides, or a deficiency in high-density lipoprotein cholesterol (HDL-C) (Haney, *et al*., 2007).

Childhood dyslipidemia is associated with the risk of developing CVD in adulthood (Kavey, *et al*., 2003). The primary known risk factors for dyslipidemia include genetic disorders of lipid metabolism such as familial hypercholesterolemia. However secondary causes of dyslipidemia in adolescents are diabetes, cigarette smoking and anorexia nervosa. In view of the rising trends in dyslipidemia in children and adolescents, there is the need to continually identify the newer risk factors for dyslipidemia in children and adolescents, especially for those with other underlying metabolic syndromes. Vitamin D deficiency is thought to be one of new risk factors for dyslipidemia in this population (Kendrick, *et al*., 2008). In vitamin D deficient youths, successful repletion of vitamin D has been shown to reduce the possibility of developing CVD in adulthood (Lee JH, *et al*., 2008). The metabolic syndrome develops in an individual with any three of the following risk factors: obesity, diabetes, inflammation, hypertension, dyslipidemia, and thrombosis. Recent evidence suggests that vitamin D may play a role in the development of some of these risk factors. Active research revealed the role of vitamin D in the development of obesity, diabetes, inflammation, and hypertension. On the other hand, limited research has been done on the role of vitamin D in other risk factors such as dyslipidemia and thrombosis (Award, *et al*., 2012).

However, to date few studies have evaluated the relationship of vitamin D deficiency with dyslipidemia, especially in children. Therefore, the objective of this study is to evaluate the association between vitamin D deficiency and blood lipids among school age Egyptian children.

Subjects And Methods:

A cross-sectional study comprised 215 children, 80(37.2%) boys and 135 (62.8%) girls. They were Pre-pubescent (tanner stage 1) aged from 9 to 11 years. The pupils were recruited from two primary public schools situated in Giza governorate in Egypt. Children were excluded if they were: below 9 or over 11years, had endocrinal and genetic obesity,or with chronic debilitating diseases: e.g. (hepatic or renal disease, diabetes mellitus, rheumatic and congenital heart diseases, hypertension and chronic lung diseases),or with metabolic diseases (metabolic rickets, calcium metabolism disorders), mal-absorptive disorders (Crohn's disease, cystic fibrosis, and celiac disease) and cancer and if they have taken medications as anticonvulsants or systemic glucocorticoids or ingestion of vitamin D or multi-vitamin supplements.

Written informed consents were obtained from parents after explanation of the aim of the study. The study was approved by the medical ethics committee of the National Research Centre.

Physical Examination:

Children were subjected to thorough clinical examination that included chest, heart, abdominal, and central nervous system examination. Assessment of pubertal development was according to Tanner's scoring (Tanner, *et al*., 1998).

The Anthropometric measurements, that include: weight, height, were performed. The height was measured to the nearest 0.1 cm using a Holtain portable anthropometer, and the weight was determined to the nearest 0.01 kg using a Seca scale Balance with the subject dressed in minimal clothes and without shoes. The BMI was calculated as weight (in kilograms) divided by height (in meters) squared. BMI- Z-score was calculated based on the WHO growth standards (WHO, 2009)with the help of Anthro-plus Program of PC.

Laboratory Determinations:

A venous blood sample was withdrawn from each child after an overnight fast of 12 hr. Serum was separated and stored at –20°C until assayed.Serum samples were assayed for 25-hydroxy vitamin D (25(OH) vitamin D) using quantitative enzyme immunoassay (Wielders and Wijnberg, 2009). Serum 25-hydroxyvitamin D [25(OH) D] is the major circulating form of vitamin D and a standard indicator of vitamin D status (Dawson-Hughes, *et al*., 2005). In the present study two categories were considered: category 1: <30 ng/ml (vitamin D deficient); category 2:≥ 30ng/ml (normal levels) (Kumar, *et al*., 2009).

For each child, a lipid profile, were determined. Total cholesterol (TC) and triglycerides (TG) were measured by quantitative enzymatic calorimetric technique (Titez, *et al*., 1982) using Bio Merieux Kit No. 61224 and No61234, respectively. Serum High density lipoprotein - cholesterol (HDL) was measured by the phosphotungstate precipitation method (Lopez-Virella, *et al*., 1977) using Merieux Kit. Serum low density lipoprotein (LDL) was calculated using the Friedewald formula (Friedewald, *et al*., 1972) (LDL = total cholesterol – HDL – triglyceride/5). Total cholesterol (TC), HDL, LDL and TG were dichotomized using the

National Cholesterol Education Program (NCEP), expert panel on cholesterol levels in children and adolescents cutoff as; High TC was defined as ≥ 180 mg/dL and that triglyceride concentration of ≥ 110 mg/dL. Low HDL < 40 mg/dL and ≥ 40 mg/dL as sufficient, and LDL concentrations of ≥ 130mg/dL be considered high for children and adolescents (NCEP., 1992; Kwiterovich, *et al.,* 2008).

Statistical Analysis:

Continuous data were expressed as mean ± standard deviation and were compared by use of student's t-test. Categorical data were expressed as frequencies and percentages, and were analyzed with the two-tailed chi-square test. Pearson's correlation analysis was conducted to evaluate the correlation between continuous exposure and continuous covariates. Odds ratios and 95% confidence intervals were calculated for the association between serum OH vitamin D and serum lipid profile. SPSS version 16 was used for all analyses. Two-sided *p-values* <0.05 were considered statistically significant.

Results:

We studied 215 children and adolescents (mean age 10.297 ± 0.65). Of the 215 subjects 37.2 % were male and 62.8 % were female. The mean BMI was 26.52 ± 5.63 of which 27.9% have BMI < 2 and 72.1% ≥ 2. Those, with serum vitamin D ≥ 30 ng/ml, were 60.5% while those with < 30 ng/ml were 39.5. Serum total cholesterol, triglyceride and low density lipoprotein were high in 36.3%, 36.7%, 20.5% of total subjects respectively. Table (1) shows the mean and the standard deviation of the different variable studied while table (2) shows the percentage of each variable category.

On comparing the means of weight, BMI, vitamin D and serum total cholesterol, triglyceride and low density lipoprotein, as regard to gender, no statistically significant differences were detected. Except the mean of serum high density lipoprotein, this was statistically significant higher in females than in males (table 3).

Those with BMI z-score < 2 had higher mean serum vitamin D than those with BMI z-score > 2 and this difference was statistically significant. Means serum total cholesterol, triglyceride and low density lipoprotein were statistically significant higher in group with BMI z-score > 2. However, no statistical significant difference was noticed between both groups as regard to high density lipoprotein (table 4).

More or less, on comparing the means of the weight and BMI as regard to vitamin D categories , it was found that they were higher in the group of vitamin D < 30 ng/ml than that of the other group and that differences were statistically significant. Also, the means of serum total cholesterol, triglyceride and low density lipoprotein were statistically significant higher in the same group (vitamin D < 30 ng/ml) compared with the other group of vitamin D (> 30ng/ml). As regard to serum high density lipoprotein, its mean was significantly higher in the category with vitamin D > 30 ng/ml compared with the other category of vitamin D (table 5).

Table (6) shows the association between serum vitamin D with BMI and lipid profile. Serum OH vitamin D was inversely associated with, BMI, serum total cholesterol, triglyceride and low density lipoprotein levels. These associations were statistically significant ($p < 0.05$). On the other hand, a statistically significant direct association was found between serum OH vitamin D and high density lipoprotein ($p< 0.05$).

The effect of vitamin D deficiency on serum lipid profile was studied in table (7). It showed that those who are exposed to vitamin D deficiency were at a higher risk of getting hypercholesterolemia, high serum triglyceride and low density lipoprotein (OR=4.324, 95%CI=2.393 – 7.816 , OR=3.788, 95%CI=2.111 – 6.798 – OR=5.937, 95%CI=2.837 – 12.424 respectively). Also those exposed to vitamin D deficiency were at a higher risk of getting low serum high density lipoprotein (OR=2.702, 95%CI=1.401 – 5.211). After adjusting for sex and BMI, a significant association was the same between vitamin D deficient subjects and hig serum total cholesterol, triglyceride and low density lipoprotein (OR= 2.912, 95%CI=1.561 – 5.435, OR=2.043, 95% CI=1.115 – 3.744, OR=4.292,95%CI=1.928 – 9.554 respectively). As regard the low level of high density lipoprotein, no significant association was found with vitamin D deficient subjects (OR=1.784, 95%CI=0.927-3.433) (table 8).

Table 1: Descriptive data of the different variables.

Variable	Minimum	Maximum	Mean	SD
Age (years)	9.0	11.0	10.297	0.654
Weight (kg)	24	89	51.88	14.95
BMI (kg/m2)	16.67	38.46	26.523	5.626
Vit D (ng/ml)	15.00	65.00	53.74	14.01
TC (mg/dL)	127	221	169.65	25.47
TG (mg/dL)	56	139	99.34	22.97
HDL (mg/dL)	32	67	47.49	8.36
LDL (mg/dL)	60	160	96.72	25.25

*SD = Standard deviation, Vit D = vitamin D, BMI = Body mass index, TC = Total cholesterol, TG = Triglyceride, HDL = High density lipoprotein, LDL = Low density lipoprotein

Table 2: Distribution of the study population in each category of the studied variables.

Variable	Frequency	Percent
Sex		
male	80	37.2
female	135	62.8
BMI Z-score		
< 2	60	27.9
≥ 2	155	72.1
Vitamin D (ng/ml)		
≥ 30	130	60.5
< 30	85	39.5
Total cholesterol (mg/dL)		
<180	137	63.7
≥ 180	78	36.3
Triglyceride (mg/dL)		
< 110	136	63.3
≥ 110	79	36.7
High density lipoprotein (mg/dL)		
≥ 40	167	77.7
< 40	48	22.3
Low density lipoprotein (mg/dl)		
< 130	171	79.5
≥ 130	44	20.5

Table 3: Comparison of the means of the different variables as regard to gender.

variable	Sex	Mean	t-test	p
Age	Male Female	10.32 ± 0.67 10.28 ± 0.65	0.383	0.702
Weight (kg)	Male Female	51.56 ± 11.03 52.07 ± 16.89	- 0.242	0.809
BMI (kg/m2)	Male Female	26.54 ± 4.90 26.52 ± 6.03	0.023	0.982
Vitamin D (ng/ml)	Male Female	35.91 ± 14.40 35.63 ± 13.82	0.138	0.891
Total cholesterol (mg/dL)	Male Female	172.31 ± 27.20 168.07 ± 24.35	1.181	0.239
Triglyceride (mg/dL)	Male Female	100.28 ± 23.88 98.79 ± 22.49	0.459	0.647
High density lipoprotein (mg/dL)	Male Female	45.83 ± 7.39 48.48 ± 8.77	- 2.273	0.024*
Low density lipoprotein (mg/dL)	Male Female	101.11 ± 26.67 94.11 ± 24.10	1.928	0.056

*P < 0.05 is significant

Table 4: Comparison of the means of different variables in relation to BMI categories.

Variable	BMI category	Mean	t-test	p
Vitamin D (ng/ml)	BMI < 2 BMI ≥ 2	50.38 ± 8.38 30.07 ± 11.39	12.545	0.000*
Total cholesterol (mg/dL)	BMI < 2 BMI ≥ 2	152.08 ± 21.12 176.45 ± 23.74	- 6.955	0.000*
Triglyceride (mg/dL)	BMI < 2 BMI ≥ 2	78.47 ± 15.08 107.42 ± 20.27	- 10.036	0.000*
High density lipoprotein (mg/dL)	BMI < 2 BMI ≥ 2	49.18 ± 7.16 46.84 ± 8.72	1.854	0.065
Low density lipoprotein (mg/dL)	BMI < 2 BMI ≥ 2	84.15 ± 21.13 101.58 ± 25.09	- 4.764	0.000*

*p < 0.05 is significant

Table 5: Comparison of the means of different variables in relation tovitamin D categories.

Variable	Vitamin D categories	Mean	t-test	p
Weight (kg)	Vit D ≥ 30 Vit D < 30	45.46 ± 13.02 61.71 ± 12.16	- 9.178	0.000*
BMI (kg/m2)	Vit D ≥ 30 Vit D < 30	24.24 ± 5.19 30.02 ± 4.34	- 8.516	0.000*
Total cholesterol (mg/dL)	Vit D ≥ 30 Vit D < 30	163.04 ± 24.05 179.76 ± 24.34	- 4.962	0.000*
Triglyceride(mg/dL)	Vit D ≥ 30 Vit D < 30	92.35 ± 21.68 110.02 ± 20.78	- 5.940	0.000*
High density lipoprotein(mg/dL)	Vit D ≥ 30 Vit D < 30	49.38 ± 6.80 44.60 ± 9.65	4.263	0.000*
Low density lipoprotein(mg/dL)	Vit D ≥ 30 Vit D < 30	89.73 ± 20.08 107.40 ± 28.54	- 5.327	0.000*

*p < 0.05 is significant

Table 6: Pearson correlation between serum vitamin D and other variables.

Variable	Vitamin D (ng/ml)	
	r	p
BMI (kg/m2)	-0.678	0.000*
Total cholesterol (mg/dL)	-0.410	0.000*
Triglyceride (mg/dL)	-0.504	0.000*
High density lipoprotein (mg/dL)	0.352	0.000*
Low density lipoprotein (mg/dL)	-0.400	0.000*

*p < 0.05 is significant

Table 7: Association between vitamin D deficiency and dyslipidemia.

Variable categories	Vitamin D categories		Total	Chi-square	OR	95% CI	p
	Vit D < 30 (low)	Vit D >30 (Normal))					
TC ≥180 (High)	48 (56.5%)	30 (23.1%)		23.369	4.324	2.393 – 7.816	0.000*
TC <180 (Normal))	37 (43.5%)	100 (76.9%)					
	85 (100%)	130 (100%)	215				
TG ≥110 (High)	47 (55.3%)	32 (24.6%)		19.513	3.788	2.111 – 6.798	0.000*
TG<110 (Normal)	38 (44.7%)	98 (75.4%)					
	85 (100%)	130 (100%)	215				
HDL <40 (Low)	28 (32.9%)	20 (15.4%)		8.151	2.702	1.401 – 5.211	0.004*
HDL ≥40 (Normal)	57 (67.1%)	110 (84.6%)					
	85 (100%)	130 (100%)	215				
LDL ≥130 (High)	32 (37.6%)	12 (9.2%)		23.781	5.937	2.837 – 2.424	0.000*
LDL <130 (Normal)	53 (62.4%)	118 (90.8%)					
	85 (100%)	130 (100%)	215				

*****p< 0.05 is significant
TC = Total cholesterol, TG = Triglyceride, HDL = High density lipoprotein, LDL = Low density lipoprotein, OR= odds ratio, CI= confidence interval

Table 8: Association between vitamin D deficiency and dyslipidemia after adjustment for sex and BMI.

Vit D <30 (low)	Chi-square	Adjusted OR	95% CI	p
TC ≥180 (High)	11.272	2.912	1.561 – 5.435	0.001*
TG ≥110 (High)	5.146	2.043	1.115 – 3.744	0.021*
HDL <40 (Low)	2.775	1.784	0.927-3.433	0.083
LDL ≥130 (High)	14.203	4.292	1.928 – 9.554	0.000*

*****p< 0.05 is significant
Vit.D= vitamin D, TC = Total cholesterol, TG = Triglyceride, HDL = High density lipoprotein, LDL = Low density lipoprotein, OR= odds ratio, CI= confidence interval

Discussion:

Our results showed statistically significant inverse association of serum OH vitamin D with BMI, serum cholesterol, triglyceride and low density lipoprotein and direct association of serum high density lipoprotein. Also, results showed significant increased odds ratio for hypercholesterolemia, hypertriglyceridemia , and high low density lipoprotein, in subjects with serum OH vitamin D less than 30 ng/ml compared with those with normal serum OH vitamin D after adjustment for sex and BMI (2.912, 95%CI=1.561 – 5.435, OR=2.043, 95% CI=1.115 – 3.744, OR=4.292,95%CI=1.928 – 9.554 respectively). For low high density lipoprotein in the deficient group of vitamin D, the odd ratio was also significantly high (2.702, 95%CI=1.401 – 5.211) but after adjustment for sex and BMI no significant association was found (OR=1.784, 95%CI=0.927-3.433).

Average serum OH vitamin D found in our study was 53.74±14.01 ng/ml and proportion of subjects having serum OH vitamin D < 30 ng/ml was 39.5%. These results are inconsistent with a cross-sectional study done on a group of Egyptian students in 2012 that showed, a mean serum OH vitamin D of 23.7±12.68 ng/ml and 74.6% had serum OH vitamin D < 30 ng/dl (Fawzi, *et al.*, 2012). The higher average level of OH vitamin D in our study could be explained by younger age-distribution of the study population. The lower serum OH vitamin D levels in the other study, is possibly due to insufficient exposure to sunlight and poor dietary intake of vitamin D by the subjects who are in the University- age. There was an inverse association between serum OH vitamin D and BMI in our study, which is in concordance with a previous study done in Egypt in 2012 (Youssef, *et al*., 2012).

Most of the epidemiological studies investigated the association between vitamin D deficiency and dyslipidemia in adults. In USA, low serum OH vitamin D was found to be associated with important cardiovascular disease risk factors including high serum triglyceride in a survey conducted by the National Center for health statistics in adults (Martins, *et al*., 2007). In a cohort British study in adults, serum OH vitamin D was found to be inversely associated with metabolic syndrome risk factors including serum triglyceride (Hyppönen, *et al*., 2008). The results of the previous two studies are comparable with our study as regard to serum OH vitamin D and triglyceride. A cross sectional study done in Norway, found a significant increase in serum total cholesterol, high density lipoprotein and low density lipoprotein with increasing serum OH vitamin D. This result is not consistent with our result as regard to totalcholesterol and low density lipoprotein but consistent with high density lipoprotein without adjustment for sex and BMI (Jorde, *et al.*, 2010). Many studies conducted in adults, showed inverse association between serum OH vitamin D and triglyceride, total cholesterol, and low density lipoprotein which are in favor of our results (Karhapää, *et al*., 2010; Hye Yin Park, *et al*., 2012; El-Menyar, *et al*., 2012).

Few epidemiologic studies were done to detect the association between serum vitamin D and dyslipidemia in children and adolescents. In 2009, a study done in USA showed a significant association between vitamin D deficiency and low levels of serum high density lipoprotein irrespective of adiposity which is consistent with our result in the unadjusted study (Kumar, *et al.*, 2009). In contrast to our study, two studies in USA were conducted on adolescents, showed no significant associations between low serum OH vitamin D and low high density lipoprotein, high triglyceride levels and low density lipoprotein (Reis, *et al*., 2009; Ashraf, *et al*., 2009). Differences in findings between our study and that of these two prior studies among youth may be due to lack of consistency in the categorization of both exposure and outcome, variations in covariate assessments such as, inadequate adjustment of confounding leading to the possibility of residual confounding, or unevaluated effect modification and differences in study population characteristics and distribution. In consistence with our study, hypertriglyceridemia was associated with increased odds of having low serum OH vitamin D levels in 2 studies done on Caucasian children and adolescents in 2011and another one on Spanish school children in the same year. In contrast to our study, the first study showed a significant association also with low high density lipoprotein which was not significant in our study after adjustment for sex and BMI (Pacifico, *et al*., 2011; Rodríguez-Rodríguez, *et al*., 2011).

Although the biological mechanism linking vitamin D deficiency to the risk ofdyslipidemia is still poorly understood, the most acceptable proposed possible indirectmechanism involves the activation of the vitamin D receptor and increasing lipoprotein lipase enzyme levels with subsequent decreasing triglyceride levels (Rejnmark, *et al*., 2010).

Our study has several limitations. We did not account for parathyroid hormone (PTH) levels. PTH levels may play a role for the effect of OHVD. However, effects of PTH levels on metabolic syndrome still remains a controversy as the previous results have been inconsistent. In one study, researchers found metabolic syndrome positively related to PTH levels in older men but not in women (Reis, *et al*., 2008) while others found no evidence of independent association between PTH levels and MS (Lee, *et al*., 2009). Another study reported results favoring PTH and not OHVD levels as an independent predictor of MS, but results were limited to morbidly obese Caucasians (Hjelmesaeth, *et al*., 2009). A more recent study showed inconsistent associations of PTH levels with MS across different OH vitamin D levels (Zhao, *et al*., 2010).

One major limitation of our cross-sectional study design, due to its observational nature, was our lack of temporality between vitamin D levels and the risk of dyslipidemia (Temporal relationship between exposure and the occurrence of the disease). Hencecausality could not be established due to the difficulty in demonstrating if the vitamin Ddeficiency preceded the dyslipidemia. Despite this inability to establish a cause-and effectrelationship, the study granted us a hypothesis generating ability. In addition, theextreme obesity of the study participants may have masked the relevant associationsbetween vitamin D deficiency and dyslipidemia. This could have happened becausevitamin D is a fat soluble vitamin, hence when in excess it is stored in body fat, thereforefor individuals who were obese and had excess fat stores, the bulk of their vitamin D mayhave been trapped and stored in the excess fat hence, increasing their risk of vitamin Ddeficiency . As such, the observed significant increase in odds of high TC, low HDL as well as high TG amongst children and adolescents with below optimal vitamin Dlevels compared to children with normal vitamin D levels, could possibly be due to

thefact that some of their serum vitamin D was being trapped within the elevated serumblood lipid levels, implying a possible reverse causality (Reinehr, *et al.*, 2007). A randomized clinical trialwould be needed to assess this possible reverse causality and thus ascertain therelationship between vitamin D and dyslipidemia in these children and adolescents.

More epidemiologic studies needed to be conducted in a larger number of children and adolescents to confirm that association between vitamin D deficiency and dyslipidemia as our study has limitation in the relatively small number of subjects involved in the study.

In summary, our findings relate vitamin D deficiency to dyslipidemia in children and add to the sparse body of literature in this area. We found that children and adolescents with varying levels of vitamin D deficiency had significantly increased risk of high total cholesterol, triglyceride and low density lipoprotein. Findings can inform more aggressive lifestyle and dietary interventions with vitamin D supplementation to reduce the risk of dyslipidemia in high risk children. Findings also shed light on the prevalence of vitamin D deficiency in this unique population of children and adolescents.

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